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10/540,784	06/08/2005	Mark E. Fraley	21301P	9106

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EXAMINER	
MOORE, SUSANNA	
ART UNIT	PAPER NUMBER
1624	
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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/540,784	FRALEY, MARK E.	
	Examiner	Art Unit	
	SUSANNA MOORE	1624	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *04 April 2008*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *37-43* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *37-39 and 43* is/are rejected.

7)☒ Claim(s) *40-42* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Response to Arguments

In summary, claims 37-43 are new claims and the only claims under consideration. This is a second Nonfinal Office Action due to new rejections being made.

Specification

The objection of the title of the invention is withdrawn based on the amendment.

Claim Objections

The objection of claims 2 and 4 for not being further limiting is withdrawn based on the amendments.

The objection of claims 1-4 and 6-9 for words which are capitalized and should be lower case is withdrawn based on the amendments.

Claim 37 is objected to because of the following informalities: the word "Unsubstituted" should be replaced with "unsubstituted." See pages 4 and 5 (bridged). Appropriate correction is required.

Claims 40-42 are objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

The rejection of claim 1 under 35 U.S.C. 112, second paragraph, as being indefinite for the terms "unsubstituted or substituted alkyl," "unsubstituted or substituted alkenyl," "unsubstituted or substituted alkenyl," is withdrawn based on the amendments.

The rejection of claim 1 under 35 U.S.C. 112, second paragraph, as being indefinite for the term “heterocyclic," is withdrawn based on the amendments.

Claims 37, 38 and 43 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The variables “a” and “b” are not defined on formula I. See claim 37, page, 3, line 5. Thus, said variables are vague.

The definition of R^a and R^b cannot be defined with itself. This is indefinite. See claim 37, page 4, lines 12 and 16.

Claim Rejections - 35 USC § 102

The rejection of claims 1-4 and 9 under 35 U.S.C. 102(b) as being anticipated by Bilodeau et. al. (US 6380203 B1) is withdrawn based on the amendments.

The rejection of claims 1-4 under 35 U.S.C. 102(b) as being anticipated by Mustazza et. al. (J. Heterocyclic Chem., 2001, 38, 1119-1129) is withdrawn based on the amendments.

The rejection of claims 1-4 under 35 U.S.C. 102(b) as being anticipated by Fraley et. al. (Bioorg. Med. Chem. Lett., 2002, 12, 2767-2770) is withdrawn based on the amendments.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.

4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

The rejection of claims 1-4 under 35 U.S.C. 103(a) as being unpatentable over Fraley et. al. (Bioorg. Med. Chem. Lett., 2002, 12, 2767-2770) is withdrawn based on the amendments.

Claims 37-39 and 43 are rejected under 35 U.S.C. 103(a) as being unpatentable over Bilodeau et. al. (US 6380203 B1).

The instant Application claims compounds of formula (I) as tyrosine kinase inhibitors, wherein R^2, R^3 and R^5= hydrogen, R^4= 4-methoxyphenyl and R^1= 5-methoxy-3-pyridyl).

The reference teaches compounds of formula (I) as tyrosine kinase inhibitors, wherein R^2, R^3 and R^5= hydrogen, R^4= 4-methoxyphenyl and R^1= 3-pyridyl, see column 10, example 1, lines 43-56.

The difference between the claimed compound and the reference is the substitution on the pyridyl at the 3-position of the bicycle, hydrogen versus Applicant's 5-methoxy. The genus of formula (I) in column 2, teaches that the heterocyclic ring at R^1 can be substituted with hydrogen, alkyl, mono- and dialkylamino, aryl, heterocyclyl, etc. See lines 56-65, in column. Furthermore, the genus also teaches R^1 can be alkyl, halo, alkenyl, alkynyl and heteroaryl substituted with COOalkyl, see column 2, lines 41-46. Thus, said claims are rendered obvious by Bilodeau et. al.

Applicant traverses the above rejection by stating, "…, a closer inspection of the claimed invention will reveal that when R^1 is a C_{5-10} hetercyclyl it must contain at least one substituent and that substituent cannot be a methoxy group. The substituents available for substitution on the C_{5-10} heterocyclyl are significantly different both structurally and chemically from the

compounds disclosed in Fraley et al. Thus, a person of ordinary skill in the art would not expect the instantly claimed compounds." This is not found persuasive because as mentioned above in the rejection, the genus teaching not only specifies a methoxy, the generic teaching in the reference teaches R^1 is alkyl, the same as claimed in the instant Application. Furthermore, there is significant overlap at R^4, see column 2, line 50. Thus, the rejection is maintained.

The applied reference has a common inventor with the instant application. Based upon the earlier effective U.S. filing date of the reference, it constitutes prior art only under 35 U.S.C. 102(e). This rejection under 35 U.S.C. 103(a) might be overcome by: (1) a showing under 37 CFR 1.132 that any invention disclosed but not claimed in the reference was derived from the inventor of this application and is thus not an invention "by another"; (2) a showing of a date of invention for the claimed subject matter of the application which corresponds to subject matter disclosed but not claimed in the reference, prior to the effective U.S. filing date of the reference under 37 CFR 1.131; or (3) an oath or declaration under 37 CFR 1.130 stating that the application and reference are currently owned by the same party and that the inventor named in the application is the prior inventor under 35 U.S.C. 104, together with a terminal disclaimer in accordance with 37 CFR 1.321(c). This rejection might also be overcome by showing that the reference is disqualified under 35 U.S.C. 103(c) as prior art in a rejection under 35 U.S.C. 103(a). See MPEP § 706.02(l)(1) and § 706.02(l)(2).

Claims 37-39 and 43 are rejected under 35 U.S.C. 103(a) as being unpatentable over Bilodeau et. al. (US 6235741 B1). The 10th specie listed in claim 3 of the reference, 3-(3-pyridyl)-6-(4-methoxyphenyl)pyrazolo(1,5-a)pyrimidine is obvious over 3-(4-amino(3-pyridyl))-

6-(4-methoxyphenyl)pyrazolo(1,5-a)pyrimidine. The only difference between the two named species is the substitution on the pyridyl ring at the 6-position of the bicycle, the amino substituent at the four position of the pyridyl ring claimed in the instant invention versus hydrogen. The genus in column 2, lines 56 and 59 teaches the variables are alternatively useable. The reference also teaches R^1 can be alkyl, alkenyl, alkynyl and heteroaryl substituted with COOalkyl, see column 2, lines 42-46 and 56-61. Thus, said claims are rendered obvious by the '741 patent.

The applied reference has a common inventor with the instant application. Based upon the earlier effective U.S. filing date of the reference, it constitutes prior art only under 35 U.S.C. 102(e). This rejection under 35 U.S.C. 103(a) might be overcome by: (1) a showing under 37 CFR 1.132 that any invention disclosed but not claimed in the reference was derived from the inventor of this application and is thus not an invention "by another"; (2) a showing of a date of invention for the claimed subject matter of the application which corresponds to subject matter disclosed but not claimed in the reference, prior to the effective U.S. filing date of the reference under 37 CFR 1.131; or (3) an oath or declaration under 37 CFR 1.130 stating that the application and reference are currently owned by the same party and that the inventor named in the application is the prior inventor under 35 U.S.C. 104, together with a terminal disclaimer in accordance with 37 CFR 1.321(c). This rejection might also be overcome by showing that the reference is disqualified under 35 U.S.C. 103(c) as prior art in a rejection under 35 U.S.C. 103(a). See MPEP § 706.02(l)(1) and § 706.02(l)(2).

Claims 37, 38 and 43 are rejected under 35 U.S.C. 103(a) as being unpatentable over Bilodeau et. al. (US 6245759 B1). The 12th specie listed in claim 2 of the reference, 1-(3-dimethylamino-propyl)-4-(3-thiophen-3-yl)pyrazolo(1,5-a)pyrimidin-6-yl-1H-pyridin-2-one is obvious over (3-thiophen-3-yl)pyrazolo(1,5-a)pyrimidin-6-yl-1H-pyridin-2-one. The only difference between the two named species is the substitution on the pyridyl ring at the 6-position of the bicycle, the 3-dimethylamino-propyl versus Applicant's hydrogen. The genus in column 27, line 32, teaches the two variables are alternatively useable. Thus, said claims are rendered obvious by the '759 patent.

The applied reference has a common inventor with the instant application. Based upon the earlier effective U.S. filing date of the reference, it constitutes prior art only under 35 U.S.C. 102(e). This rejection under 35 U.S.C. 103(a) might be overcome by: (1) a showing under 37 CFR 1.132 that any invention disclosed but not claimed in the reference was derived from the inventor of this application and is thus not an invention "by another"; (2) a showing of a date of invention for the claimed subject matter of the application which corresponds to subject matter disclosed but not claimed in the reference, prior to the effective U.S. filing date of the reference under 37 CFR 1.131; or (3) an oath or declaration under 37 CFR 1.130 stating that the application and reference are currently owned by the same party and that the inventor named in the application is the prior inventor under 35 U.S.C. 104, together with a terminal disclaimer in accordance with 37 CFR 1.321(c). This rejection might also be overcome by showing that the reference is disqualified under 35 U.S.C. 103(c) as prior art in a rejection under 35 U.S.C. 103(a). See MPEP § 706.02(l)(1) and § 706.02(l)(2).

Claims 37, 38 and 43 are rejected under 35 U.S.C. 103(a) as being unpatentable over DeFeo-Jones et. al. (US 20020041880 A1).

The instant Application claims compounds of formula (I), wherein R^2, R^3 and R^5= hydrogen, R^4= 4-methoxyphenyl and R^1= alkyl and heterocyclyl substituted with a COOalkyl.

The reference teaches compounds of formula (I), wherein R^2, R^3 and R^5= hydrogen, R^4= 4-methoxyphenyl and R^1= thienyl. See page 46, example 1, bottom of left-hand column.

The only difference between the two named species is the substitution at R1, thienyl versus Applicant's alkyl and heterocyclyl substituted with a COOalkyl. The genus on page 6, left-hand column, paragraph 0056, 0060 and 0062. The genus in the reference teaches these variables are alternatively useable. This is just one example in the reference which renders the instant Application obvious. Thus, said claims are rendered obvious by DeFeo-Jones et. al.

The applied reference has a common inventor with the instant application. Based upon the earlier effective U.S. filing date of the reference, it constitutes prior art only under 35 U.S.C. 102(e). This rejection under 35 U.S.C. 103(a) might be overcome by: (1) a showing under 37 CFR 1.132 that any invention disclosed but not claimed in the reference was derived from the inventor of this application and is thus not an invention "by another"; (2) a showing of a date of invention for the claimed subject matter of the application which corresponds to subject matter disclosed but not claimed in the reference, prior to the effective U.S. filing date of the reference under 37 CFR 1.131; or (3) an oath or declaration under 37 CFR 1.130 stating that the application and reference are currently owned by the same party and that the inventor named in the application is the prior inventor under 35 U.S.C. 104, together with a terminal disclaimer in

accordance with 37 CFR 1.321(c). This rejection might also be overcome by showing that the reference is disqualified under 35 U.S.C. 103(c) as prior art in a rejection under 35 U.S.C. 103(a). See MPEP § 706.02(l)(1) and § 706.02(l)(2).

Claims 37, 38 and 43 are rejected under 35 U.S.C. 103(a) as being unpatentable over Bellec et. al. (J. of Heterocyclic Chemistry, 1995, 32(6), 1793-1800).

The instant Application claims compounds of formula (I), wherein R^2, R^3 and R^5= hydrogen, R^4= phenyl and R^1= methyl.

The reference teaches compounds of formula (I), wherein R^2= methyl, R^3 and R^5= hydrogen, R^4= phenyl and R^1= hydrogen. See page 1794, Table 1, compound 1c.

The only difference between the two named species is the substitution at R1 and R2, hydrogen versus methyl (switched at each position). These compounds are positional isomers and homologues. Since a methyl group is considered a homolog of hydrogen these compounds are considered equivalent. The MPEP 2144.09 states "Compounds which are position isomers (compounds having the same radicals in physically different positions on the same nucleus) or homologs (compounds differing regularly by the successive addition of the same chemical group, e.g., by -CH2- groups) are generally of sufficiently close structural similarity that there is a presumed expectation that such compounds possess similar properties. In re Wilder, 563 F.2d 457, 195 USPQ 426 (CCPA 1977).

Thus, said claims are rendered obvious by Bellec et. al.

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 37-39 and 43 are rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claim1-3 of U.S. Patent No. 6235741. Although the conflicting claims are not identical, they are not patentably distinct from each other because the '741 patent contains obvious variants of the species embraced by the genus of the instant Application. For example, the 10th specie listed in claim 3 of the reference, 3-(3-pyridyl)-6-(4-methoxyphenyl)pyrazolo(1,5-a)pyrimidine is obvious over 3-(4-amino(3-pyridyl))-6-(4-methoxyphenyl)pyrazolo(1,5-a)pyrimidine. The only difference between the two named species is the substitution on the pyridyl ring at the 6-position of the bicycle, the amino substituent at the four position of the pyridyl ring claimed in the instant invention versus hydrogen. The genus in column 2, lines 56 and 59 teaches the variables are alternatively useable. Thus, said claims are rendered obvious by the '741 patent.

Applicant traverses the above rejection by stating, "The amino substituted compound is not specifically claimed by Applicants. Additionally, one of ordinary skill would not readily expect that a compound having an amino substitution versus a compound having a hydrogen substitution to be equivalent without experimentation. It is known in the art that the addition of a substituent such as an amino group could impart significantly different properties on a compound when compared to a hydrogen group. The two compounds are both structurally and chemically different and their activity as tyrosine kinase inhibitors cannot be predicted by merely observing the structure." This is not found persuasive since this is just one example that was used to compare a specific specie from the reference and the instant Application. For example, the generic teaching in the '741 patent teaches R^1 is alkyl, the same as claimed in the instant

Application, see column 2, line 43. Furthermore, there is significant overlap at R^4, see column 2, line 50. Thus, the rejection is maintained.

Claims 37, 38 and 43 are rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claim1-3 of U.S. Patent No. 6245759. Although the conflicting claims are not identical, they are not patentably distinct from each other because the '759 patent contains obvious variants of the species embraced by the genus of the instant Application. For example, the 12th specie listed in claim 2 of the reference, 1-(3-dimethylamino-propyl)-4-(3-thiophen-3-yl)pyrazolo(1,5-a)pyrimidin-6-yl-1H-pyridin-2-one is obvious over (3-thiophen-3-yl)pyrazolo(1,5-a)pyrimidin-6-yl-1H-pyridin-2-one. The only difference between the two named species is the substitution on the pyridyl ring at the 6-position of the bicycle, the 3-dimethylamino-propyl versus Applicant's hydrogen. The genus in column 27, line 32, teaches the two variables are alternatively useable. Thus, said claims are rendered obvious by the '759 patent.

Applicant traverses the above rejection by stating, "Applicants do not specifically claim the unsubstituted pyridyl compound. Additonally, one of ordinary skill would not readily expect that these compounds would be equivalent without experimentation since they are structurally and chemically different. It is known in the art that the addition of a substituent such as a dimethylamino-propyl could impart significantly different properties on a compound when compared to no substitution. The two compounds are both structurally and chemically different and their activity as tyrosine kinase inhibitors cannot be predicted by merely observing the structure." This is not found persuasive since firstly, the pyridyl is not unsubstituted. The pyridyl

has a ketone which tautomerizes to a hydroxyl substituted pyridyl, which Applicant is claiming. Moreover, R^1 can be an alkyl, alkenyl and alkynyl, see column 4, lines 15, as taught by the '759 patent. Thus, the rejection is maintained.

Claims 37-39 and 43 are rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claim1-3 of U.S. Patent No. 6380203. Although the conflicting claims are not identical, they are not patentably distinct from each other for the same reason cited in the 103 art rejection above.

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to SUSANNA MOORE whose telephone number is (571)272-9046. The examiner can normally be reached on M-F 8:00-5:00 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, James Wilson can be reached on (571) 272-0661. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Susanna Moore/
Examiner, Art Unit 1624

/Brenda L. Coleman/
Primary Examiner, Art Unit 1624